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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,055	11/16/1999	YOSHIHIRO USUDA	0010-1057-0	3806
22850 7590 02/07/2008 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314				
			EXAMINER FRONDA, CHRISTIAN L	
			ART UNIT 1652	PAPER NUMBER
			NOTIFICATION DATE 02/07/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No. 09/441,055	Applicant(s) USUDA ET AL.	
	Examiner Christian L. Fronda	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31,35 and 41-59 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31,35 and 41-59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>11/21/07</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Claims 31, 35, and 41-49 are pending and under consideration in this Office Action.
2. References AO and AP cited in the PTO form 1449 of the IDS filed 11/21/2007 have not been considered because English translations of these Japanese patents have not been provided.

Claim Rejections - 35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
4. Claims 31, 35, and 41-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Michaeli et al. (Advances in Polyamine Research (1983), 4, 519-20; reference of record PTO 892) in view of the combined teachings of Greene (Escherichia coli and Salmonella Cellular and Molecular Biology, 2nd Edition, pps. 542-560, "BIOSYNTHESIS OF METHIONINE", 1996; PTO 1449 of IDS dated 02/16/2000) and Park et al. (Bioorg Med Chem. 1996 Dec;4(12):2179-85). The rejection of record is reproduced below.

Michaeli et al. teach a process for producing L-methionine comprising culturing recombinant strains of *E.coli* having multicopy plasmids containing the metA gene which codes for homoserine transsuccinylase, the first enzyme in the methionine biosynthesis pathway (see entire publication).

The claims differ from the teachings of Michaeli et al. in that Michaeli et al. does not teach the a recombinant *Escherichia* bacterium deficient in the metJ gene encoding a repressor of the L-methionine biosynthesis system.

Greene teaches the *E.coli* repressor of the L-methionine biosynthesis system encoded by the metJ gene (see entire publication, especially p. 552).

Park et al. teach the enzyme *E.coli metK* gene encoding S-adenosylmethionine synthetase

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which catalyzes the synthesis of S-adenosyl-L-methionine (SAM), where SAM is a major methyl group transfer agent in biological systems and the methyl moiety of SAM is transferred to proteins, lipids, nucleic acids, and vitamins by SAM-dependent methyltransferases (see abstract and entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the process of Michaeli et al. such that the metJ gene taught by Greene is inactivated in order to make the recombinant *E. coli* having multicopy plasmids containing the metA gene taught by Michaeli et al. deficient in the *E. coli* repressor of the L-methionine biosynthesis system and reduce activity of the intracellular S-adenosylmethionine synthetase taught by Park et al.. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of having a simple culturing method that produces L-methionine, where inactivation of the metJ gene encoding the *E. coli* repressor of the L-methionine biosynthesis system would lead to increased amounts of produced L-methionine and reduced intracellular S-adenosylmethionine synthetase leads to reduced transfer of methyl moieties for the production of SAM by action of S-adenosylmethionine synthetase. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since recombinant molecular biology techniques for inactivating genes are well known and developed in the art.

The arguments filed 10/31/2007 have been fully considered but are not persuasive for reasons of record as supplemented below. It must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The examiner recognizes that obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Furthermore, in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. —, 82 USPQ2d 1385, 1397 (2007) the U.S. Supreme Court held that "The obviousness analysis cannot be confined by formalistic conception of the words, teachings, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents" (at 1396).

The obviousness rejection of record combines prior art elements according to known methods to yield predictable results. One of ordinary skill in the art at the time the invention was

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made would have been motivated to modify the reference teachings of Michaeli et al. as stated above for the purposes of having a simple culturing method that produces L-methionine. One of ordinary skill in the art at the time the invention was made would recognize that substrates and precursor substrates sequestered for other metabolic pathways leading away from the metabolic pathways for production of L-methionine would inherently lead to decreased or no production L-methionine. One of ordinary skill in the art would recognize that inactivating the activity of enzymes and proteins that inhibit the production of L-methionine such as the MetJ repressor, inactivating the activity of enzymes and proteins that sequester substrates and precursor substrates away from the metabolic pathways for production of L-methionine, increasing the activity of enzymes and proteins in the metabolic pathways for production of L-methionine, and desensitizing of enzymes metabolic pathways for production of L-methionine to any type of inhibition would inherently lead to production of L-methionine. Therefore, the method steps recited in the claims is within the purview of one of ordinary skill in the art, where the limitations of the method steps would lead to increased production of L-methionine.

Conclusion

5. No claim is allowed.

6. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday- Friday from 9:00AM - 5:00PM. If attempts to reach

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the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N. Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

8. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000. CLF


TEKCHAND SAIDHA
PRIMARY EXAMINER